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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,858	04/26/2006	Kirsten Ebbehoj	50412/022002	5360
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CLARK & ELBING LLP 101 FEDERAL STREET BOSTON, MA 02110				
EXAMINER				
CHANDRA, GYAN				
ART UNIT		PAPER NUMBER		
1646				
NOTIFICATION DATE		DELIVERY MODE		
05/05/2008		ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary

Application No.

10/529,858

Applicant(s)

EBBEHOJ ET AL.

Examiner

GYAN CHANDRA

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Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 February 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 67 and 69-108 is/are pending in the application.
- 4a) Of the above claim(s) 70, 86-88, 97, 98 and 103-106 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 67, 69, 71-85, 89-96, 99-102, 107 and 108 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsman's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 2/15/2008
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group 1, and a single polypeptide (des Pro36, Pro37, Pro38, [Asp28] Exendin-4(1-39)-(Lys)6-NH2) in the reply filed on 2/15/2008 is acknowledged. The traversal is on the ground(s) that claim 67 is the only independent claim which recites a class of peptides containing an asp, an isoaspartyl, or a cyclic imide at position 28 of the exendin-4 sequence and therefore, all claimed polypeptide have common structural feature. Applicants further argue that in view of common features, searching for the claimed peptides would not be non-coextensive searches. This is not found persuasive because claimed sequences do not share common structure, for example cyclic imide at position 28 is not the same structure (special technical feature) as an aspartic acid (amino acid). Further the polypeptide exendin-4 having a single amino acid change at position 28 does not require the special technical features of Met(O)14, Trp(O2)25, cyclic imide28 or a combination thereof as recited in many claims. Applicants arguments that at least a single polypeptide des Pro36, Pro37, Pro38, [Asp28] Exendin-4(1-39)-(Lys)6-NH2 should be examined is found persuasive therefore, the elected polypeptide des Pro36, Pro37, Pro38, [Asp28] Exendin-4(1-39)-(Lys)6-NH2 and [asp28]-exendin-4 would be examined together.

The requirement is still deemed proper and is therefore made FINAL.

Status of Application, Amendments, And/Or Claims

Claims 67, 69-108 are pending.

Claims 70, 86-88, 97-98, 103-106 are withdrawn for reciting non-elected inventions (e.g., oxydized methionine or oxidized tryptophan or peptide sequences).

Claims 67, 69, 71-85, 89-96, 99-102, and 107-108 are examined to the extent they read on elected sequence (i.e., [asp28] extendin-4 or des Pro36, Pro37, Pro38, [Asp28] Extendin-4(1-39)-(Lys)6-NH2).

Sequence Compliance

The disclosure of nucleotide and/or amino acid sequences which are not in the sequence compliance as per 37 CFR 1.821-1.825. The sequence rules embrace all unbranched nucleotide sequences with ten or more bases and all unbranched, non-D amino acid sequences with four or more amino acids, provided that there are at least 4 "specifically defined" nucleotides or amino acids. The rules apply to all sequences in a given application, whether claimed or not (see MPEP 2421.02). It should be noted, though, that when a sequence is presented in the disclosure (through out the specification, in particular pages 12-16, 20-21, 33-36) or in Figures (Figure 9), regardless of the format or the manner of presentation of that sequence in the disclosure, the sequence must still be included in the Sequence Listing and the sequence identifier ("SEQ ID NO:X") must be used to refer the sequence. See MPEP 2422.02 under the title "The Requirement for Exclusive Conformance; Sequences Presented in Drawing Figures".

Information Disclosure Statement

The information disclosure statement (IDS) filed on 2/15/2008 have been considered.

Claim Objections

Claims 67, 75, 77, 83, 92, 101-102, and 107-108 are objected for reciting non-elected invention (i.e., non elected polypeptides; or diseases such as metabolic disorders, gastric emptying or eating disorders of Group 3).

Claims 69, 71-74, 76, 78-82, 84-85, 89-91, 93-96, 99 and 100 are objected for directly or indirectly depending from an objected or withdrawn claim.

The Examiner suggests that syntax of claims 79, 101, 102 can be improved by amending the claims as following:

In claim 79, replace "67 and 70-78" with 67, 70-77 or 78"

In claims 101 and 102, line 3: delete "30" from "30 hyperglycemia"

In claim 102, delete "stimulating insulin release" because it is a property of the compound which releases insulin in a subject when a compound is administered in said subject. This is not a disease or symptom that can be treated by administering said compound in said subject.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

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art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 67, 69, 71-85, 89-96, 99-102, and 107-108 are rejected under 35

U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising a polypeptide [asp28]exendin-4, does not reasonably provide enablement for a stabilized exendin-4 compound such as des Pro36, Pro37, Pro38, [Asp28]exendin-4 or a deletion of 1-5 amino acids corresponding to 34-38. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to which the invention commensurate in scope with these claims.

In *In re Wands*, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include: (1) Nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the breadth of the claims, (7) the quantity of experimentation needed, (8) relative skill of those in the art.

The instant disclosure fails to meet the enablement requirement for the following reasons:

The instant claims are broadly drawn to a composition a stabilized exendin-4 (1-39) comprising a deletion of 0-5 amino acids at positions corresponding to positions 34-38.

The state of the prior art and the predictability or lack thereof in the art:

Goke et al (J. Biol. Chem. 1993, 268, 19650-19655) teach that exendins are polypeptides that lower blood glucose levels and have some sequence similarity (53%) with glucagon like peptide-1 (GLP-1) (page 19650, right column). Exendins are found in

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the venom of Helodermatidae suspectum (or in beaded lizards). Exendin-3 and Exendin-4 are known to have therapeutic use for treating diabetes. The skill of stabilizing small peptide such as GLP-1 by attaching lipophilic molecules is known in the art (IDS, WO 99/43708). Further, the skill of making a mutation in a protein is well known in the art. The art does not disclose how to stabilize any peptide or protein where a deletion of 1, 2, 3, 4 or even 5 amino acids would make a protein any more stable than the parent protein. Therefore, making a variant of a peptide or protein that would increase the stability of said peptide or protein in a composition is highly unpredictable.

The amount of direction and guidance present and the presence or absence of working examples:

Given the teachings of unpredictability found in the art, detailed teachings are required to be present in the disclosure in order to enable the skilled artisan to practice the invention commensurate in scope with the claims. These teachings are absent. The specification on page 34 discloses a method of making [Asp28] Exendin (compound 10). The specification discloses administering [Asp28] Exendin-4 in db/db mice for oral glucose tolerance test (Figure 8). The instant invention is drawn to a composition of stabilized exendin-4. The specification does not provide any data that shows that the instant compounds such as [Asp28] Exendin-4, Pro36, Pro37, Pro38 [Asp28] Exendin-4 or 1-5 amino acid deletion of Exendin-4 is any more stable than a composition comprising Exendin-4. Therefore, it is unpredictable how one of the skill in the art can practice the instantly claimed invention.

The breadth of the claims and the quantity of experimentation needed: Due to the large amount of experimentation necessary to use the instant peptides to stabilize a composition than Exendin-4, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to same, the state of the prior art which establishes the unpredictability about making a more stable composition of the instant compounds than Exendin-4, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 89, 90 and 91 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 89, 90 and 91 recite the limitation "the conditions" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GYAN CHANDRA whose telephone number is (571)272-2922. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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18 April 2008
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/Robert Landsman/
Primary Examiner, Art Unit 1647